EODM DTO) 1440/A and B (N	lodifie	d)	APPLICATION NO.:	10/821,813	ATTY. DOCKET NO.:	P0453.70112US01	
FORM PTO-1449/A and B (Modified) INTORNALION BESCHOSHRE SHATEMENT RELECTED PROFESSIONT				FILING DATE:	April 8, 2004	CONFIRMATION NO	.: 9059	
				APPLICANT:	Boyd et al.			
				GROUP ART UNIT:	1614	EXAMINER:	Not Yet Assigned	
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U.S. PATENT DOCUMENTS

	Examiner's	Cite	U.S. Patent Document		Name of Patentee or Applicant of Cited	Date of Publication or of issue	
	Initials	No.	Number	Kind Code	Document	of Cited Document MM-DD-YYYY	
	OPE	A55	5,804,595		Portoghese, et al.	09-08-1998	
	MG C	A56	5,866,154		Bahal, et al.	02-02-1999	
	430 9004	A57	2003-0022909	A1	Moss, et al.	01-30-2003	
3	DEL 1 1 2001	SA 58	2003-0124086	Al	Bentley, et al.	07-03-2003	
B	MG	A59	2003-0191147	Al	Sherman, et al.	10-09-2003	
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FOREIGN PATENT DOCUMENTS

Examiner's	Cite	Foreign Patent Document			Name of Patentee or Applicant of Cited	Date of	Translation
Initials	No.	Office/ Country	Number	Kind Code	Document (not necessary)	Publication of Cited Document MM-DD-YYYY	(Y/N)
MG	B28	28 CA 2,064,37	2,064,373	73	Lilly (Eli) and Company	09-30-1992	
	B29	EP	506,468	Al	Eli Lilly and Company	09-30-1992	
	B30	EP	643,967	A2	Euro Celtique S.A.	03-22-1995	
	B31	wo	01/32180	A2	Rodeva Limited	05-10-2001	
	B32	wo	02/098422	Al	University of Chicago	12-12-2002	
V	B33	wo	03/032990	A2	Shearwater Corporation	04-24-2003	
MG	B34	wo	2004/014291	A2	Moss	02-19-2004	

OTHER ART - NON PATENT LITERATURE DOCUMENTS

Examiner's Initials	Cite No	Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s), publisher, city and/or country where published.	Translation (Y/N)
MG	C147	FARTHING et al., New drugs in the management of the irritable bowel syndrome. Drugs. 1998 Jul;56(1):11-21. Review.	
	C148	FINGL et al., Chapter 43: Laxatives and cathartics. In Pharmacological Basis of Therapeutics. 1980: 1002-5.	
	C149	SCHUBERT-ZSILAVECZ et al., Das reizdarmsyndrom irritable bowel syndrome. Deutsche apotheker zeitung. 2002 Aug 22; 142(34): 40-9. German.	Yes
V	C150	TALLEY et al., Pharmacologic therapy for the irritable bowel syndrome. Am J Gastroenterol. 2003 Apr;98(4):750-8. Review.	
MG	C151	THOMPSON et al., Laxatives: clinical pharmacology and rational use. Drugs. 1980 Jan;19(1):49-58. Review.	

EXAMINER:	DATE CONSIDERED:
/Michel Graffeo/	12/06/2006

#EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

[NOTE - The Office hereby waives the requirement under 37 CFR 1.98 (a)(2)(i) for submitting a copy of each cited U.S. patent and each U.S. patent application publication for all U.S. national patent applications filed after June 30, 2003 and for all international applications that have entered the national stage under 35 USC 371 after June 30, 2003. See 37 CFR 1.491(b). For all patent applications filed on or before June 30, 2003, copies of cited U.S. patents and patent application publications are still required unless an eIDS is filed. Copies of all other patent(s), publication(s), or other information listed must still be provided, even if it was previously submitted to, or cited by, the U.S. Patent Office in an earlier application, unless the earlier application is identified by the IDS and is relied upon for an earlier filing date under 35 U.S.C. §120, and the copy was provided in the earlier application.] Wolf, Greenfield & Sacks, P.C. | 600 Atlantic Avenue | Boston, Massachusetts 02210-2206

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[•]a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. __, filed __, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

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A and B c	E	CO/SB/08)	APPLICATION NO.:	10/821,813	ATTY. DOCKET NO	.: P0453.70112US01
	•		FILING DATE:	April 8, 2004	CONFIRMATION NO	D.: 9059
			APPLICANT:	Boyd et al.		
i	of	1	GROUP ART UNIT:	1614	EXAMINER:	Michel Graffeo
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U.S. PATENT DOCUMENTS

Examiner's Initials #	Cite	U.S. Patent Doc	ument	Name of Patentee or Applicant of Cited	Date of Publication or Issue	
	No.	Number	Kind Code	Document	of Cited Document MM-DD-YYYY	
MG		5,159,081		Cantrell et al.	10-27-1992	
					<u> </u>	

FOREIGN PATENT DOCUMENTS

Examiner's	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited	Date of Publication of	Translation
Initials #		Office/ Country	Number	Kind Code	Document	Cited Document MM-DD-YYYY	(Y/N)
MG		EP	0 289 070		Duphar International Research B.V.	11-02-1988	
				<u> </u>			
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OTHER ART — NON PATENT LITERATURE DOCUMENTS

Examiner's Initials #	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Translation (Y/N)
MG		HOFMANN et al., Hypocalcemia during restraint stress in rats. Indication that gastric ulcer prophylaxis by exogenous calcium interferes with calcitonin release. Res Exp Med (Berl). 1979 May 30;175(2):159-68.	

EXAMINER: /Michel Graffeo/	DATE CONSIDERED: 12/06/2006

[NOTE - No copies of U.S. patents, published U.S. patent applications, or pending, unpublished patent applications stored in the USPTO's Image File Wrapper (IFW) system, are included. See 37 CFR §1.98 and 1287OG163. Copies of all other patent(s), publication(s), unpublished, pending U.S. patent applications, or other information listed are provided as required by 37 CFR §1.98 unless 1) such copies were provided in an IDS in an earlier application that complies with 37 CFR §1.98, and 2) the earlier application is relied upon for an earlier filing date under 35 U.S.C. §120.]

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INFORMATION DISCLEMENT STATEMENT BY APPLICANT

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APPLICATION NO.: 10/821,813

ATTY. DOCKET NO.: P0453.70112US01

FILING DATE:

April 8, 2004

CONFIRMATION NO.: 9059

APPLICANT:

Boyd et al.

GROUP ART UNIT: 1614

EXAMINER: Not Yet Assigned

U.S. PATENT DOCUMENTS

Examiner's	Cite	U.S. Patent Doc	ument	Name of Patentee or Applicant of Cited	Date of Publication or of issue of Cited Document	
initials	No.	Number	Kind Code	Document	MM-DD-YYYY	
MG	A30	4,311,833		Namikoshi, et al.	01-19-1982	
	A31	4,377,568		Chopra, et al.	03-22-1983	
	A32	4,385,078		Onda, et al.	05-24-1983	
1	A33	4,457,907	_	Porter, et al.	07-03-1984	
	A34	4,462,839		McGinley, et al.	07-31-1984	
	A35	4,518,433		McGinley, et al.	05-21-1985	
	A36	4,556,552		Porter, et al.	12-03-1985	
	A37	4,606,909		Bechgaard, et al.	08-19-1986	
	A38	4,615,885		Nakagame, et al.	10-07-1986	
	A39	4,670,287		Tsuji, et al.	06-02-1987	
	A40	4,857,833		Sherman, et al.	08-15-1999	
	A41	4,888,346		Bihari, et al.	12-19-1989	
	A42	5,426,112		Zagon, et al.	06-20-1995	
	A43	5,536,507		Abramowitz, et al.	07-16-1996	
	A44	5,567,423		Ying, et al.	10-22-1996	
	A45	5,591,433		Michael, et al.	01-07-1997	
	A46	5,597,564		Ying, et al.	01-28-1997	
	A47	5,609,871		Michael, et al.	03-11-1997	
	A48	5,614,222		Kaplan, et al.	03-25-1997	
	A49	5,626,875		Ballester Rodes, et al.	05-06-1997	
	A50	5,629,001	_	Michael, et al.	05-13-1997	
	A51	6,025,154		Li, et al.	02-15-2000	
\/	A52	6,353,004	BI	Farrar, et al.	03-05-2002	
	A53	6,469,030	B2	Farrer, et al.	10-22-2002	
MG	A54	2001/0036951	Al	Farrar, et al.	11-01-2001	

FOREIGN PATENT DOCUMENTS

Examiner's	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of	Translation
Initials		Office/ Country	Number	Kind Code	. (not necessary)	Cited Document MM-DD-YYYY	(Y/N)
MG	B22	AU	758,416		Arch Development Corp.	07-03-1999	
	B23	CA	2,312,234		Arch Development Corp.	05-14-1999	
	B24	DE	3,780,819				
\/	B25	EP	1,047,726	A1	Quest International B.V.	07-22-1999	<u></u>
	B26	wo	99/22737	A1	Arch Development Corp.	05-14-1999	
MG	B27	wo	04/043964	A2	Mallinckrodt	05-27-2004	

FORM PTO	O-1449/A and B (M	lodifie	d)	APPLICATION NO.:	10/821,813	ATTY. DOCKET NO.: P0453.70112US01
INFO	RMATION D	ISC	LOSURE	FILING DATE:	April 8, 2004	CONFIRMATION NO.: 9059
STAT	TEMENT BY	APP	LICANT	APPLICANT:	Boyd et al.	
Sheet	12	of	3	GROUP ART UNIT:	1614	EXAMINER: Not Yet Assigned

OTHER ART — NON PATENT LITERATURE DOCUMENTS

Examiner's Initials	Cite No	Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s), publisher, city and/or country where published.	Translation (Y/N)
MG	C117	ALTIER et al., Opioid receptors in the ventral tegmental area contribute to stress-induced analgesia in the formalin test for tonic pain. Brain Res. 1996 Apr 29;718(1-2):203-6.	
	C118	BAKER et al., Functional effects of systemically administered agonists and antagonists of mu, delta, and kappa opioid receptor subtypes on body temperature in mice. J Pharmacol Exp Ther. 2002 Sep;302(3):1253-64.	
	C119	BASILISCO et al., Oral naloxone antagonizes loperamide-induced delay of orocecal transit. Dig Dis Sci. 1987 Aug;32(8):829-32.	
	C120	BASILISCO et al., Effect of loperamide and naloxone on mouth-to-caecum transit time evaluated by lactulose hydrogen breath test. Gut. 1985 Jul;26(7):700-3.	
	C121	BOWEN et al., Antagonism of the antinociceptive and discriminative stimulus effects of heroin and morphine by 3-methoxynaltrexone and naltrexone in rhesus monkeys. J Pharmacol Exp Ther. 2002 Jul;302(1):264-73.	
	C122	BOWEN et al., College on Problems of Drug Dependence 64th Annual Scientific Meeting. June 8-13, 2002. Quebec City, Quebec, Canada. Abstracts. Drug Alcohol Depend. 2002 May 1;66 Suppl 1:S1-220. Abstract No. 65.	
	C123	CARR et al., Naltrexone antagonizes the analgesic and immunosuppressive effects of morphine in mice. J	
	C124	CHOI et al., Opioid antagonists: a review of their role in palliative care, focusing on use in opioid-related constination. J Pain Symptom Manage, 2002 Jul;24(1):71-90. Review.	
	C125	CHOI et al., Inhibition of chemokine-induced chemotaxis of monkey leukocytes by mu-opioid receptor agonists. In Vivo. 1999 Sep-Oct; 13(5):389-96.	
	C126	DE PONTI et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review.	
	C127	FLORES et al., Mechanisms of morphine-induced immunosuppression: effect of acute morphine administration on lymphocyte trafficking. J Pharmacol Exp Ther, 1995 Mar;272(3):1246-51.	
	C128	GILES et al., Quaternary opiate antagonists lower blood pressure and inhibit leucine-enkephalin responses. Eur J Pharmacol. 1983 Nov 25;95(3-4):247-52.	
	C129	HO et al., Suppression of immunological functions in morphine addicted mice. NIDA Res Monogr. 1986;75:599-602.	
	C130	KEHLET et al., Review of postoperative ileus. Am J Surg. 2001 Nov;182(5A Suppl):3S-10S. Review.	
	C131	KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1999 Feb;10(1):1-13.	
	C132	KOSTIC, CAS Abstract Document No. 127: 13345, 1997.	
	C133	LI et al., Methadone enhances human immunodeficiency virus infection of human immune cells. J Infect Dis. 2002 Jan 1;185(1):118-22. Epub 2001 Dec 14.	
	C134	MACK, Paralytic ileus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101.	 -
	C135	NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse (1980) 1(2): 177-83. PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AIDS; National Institute of Drug	
	C136	Research 96: Monograph Series. U.S. Department of Health and Human Services; 1990. QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1	<u> </u>
	C137	plasma RNA level in patients with HIV infection. Eur J Pain. 2001;5(4):415-20. SAKURADA et al., Differential antagonism of endomorphin-1 and endomorphin-2 supraspinal antinociception	
	C138	hy nelevenezing and 3-methylpaltrevene Pentides 2002 May 23(5):895-901.	
	C139	SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;97(4):966-71.	
	C140	SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun. 1987 Dec;1(4):318-28.	-
\/	C141	SOLDANI et al., Central and peripheral involvement of mu receptors in gastric secretory effects of opioids in the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.	
	C142	STEINBROOK et al., An opioid antagonist for postoperative ileus, N Engl J Med. 2001 Sep 27;345(13):988-9.	
	C143	WEI et al., Abstracts of the 2002 Annual Meeting of the American Society for Clinical Pharmacology and	
MG		Therapeutics. Atlanta, Georgia, USA. March 24-27, 2002. Clin Pharmacol Ther. 2002 Feb;71(2):P1-136.	

FORM PTO)-1449/A and B (M	lodifie	d)	APPLICATION NO.:	10/821,813	ATTY. DOCKET NO.: P0453.70112US01
INFO	RMATION D	OISC	LOSURE	FILING DATE:	April 8, 2004	CONFIRMATION NO.: 9059
STAT	EMENT BY	APP	LICANT	APPLICANT:	Boyd et al.	
				GROUP ART UNIT:	1614	EXAMINER: Not Yet Assigned
Sheet	3	of	3		-	

MG	C144	WILMORE et al., Can we minimize the effects of opioids on the bowel and still achieve adequate pain control? Am J Surg. 2001 Nov;182(5A Suppl):1S-2S.	
MG	C145	WYBRAN et al., Suggestive evidence for receptors for morphine and methionine-enkephalin on normal human blood T lymphocytes. J Immunol. 1979 Sep;123(3):1068-70.	
MG	C146	YUAN, Clinical Status of Methylnaltrexone, A New Agent to Prevent and Manage Opioid-Induced Side Effects. J Support Oncol. 2004 Mar/Apr: 2(2):111-22:	

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APPLICATION NO.: 10/821,813 ATTY. DOCKET NO.: P0453.70112US01 INFORMATION DISCLOSURE STATEMENT BY APPLICANT Sheet 1 of 6 APPLICATION NO.: 10/821,813 ATTY. DOCKET NO.: P0453.70112US01 FILING DATE: April 8, 2004 CONFIRMATION NO.: Not Yet Assigned APPLICANT: Boyd et al. GROUP ART UNIT: Not Yet Assigned EXAMINER: Not Yet Assigned

U.S. PATENT DOCUMENTS

Examiner's	Cite	U.S. Patent Do	cument	Name of Patentee or Applicant of Cited	Date of Publication or of issue
Initials	No.	Number	Kind Code	Document	of Cited Document MM-DD-YYYY
MG	A1	2001/0018413	A1	Crain, et al.	08-30-2001
1	A2	2002/0028825	Al	Foss, et al.	03-07-2002
	A3	2001/0033865	A1	Oshlack, et al.	10-25-2001
	A4	2001/0036476	A 1	Oshlack, et al.	11-01-2001
	A5	2001/0047005	A1	Farrar, et al.	11-29-2001
	A6	4,176,186		Goldberg, et al.	11-27-1979
	A7	4,719,215		Goldberg	01-12-1988
	A8	4,861,781		Goldberg	08-29-1989
	A9	4,987,136		Kreek, et al.	01-22-1991
	A10	5,102,887		Goldberg	04-07-1992
	A11	5,270,328		Cantrell, et al.	12-14-1993
	A12	5,472,943		Crain, et al.	12-05-1995
	A13	5,512,578		Crain, et al.	04-30-1996
	A14	5,767,125		Crain, et al.	06-16-1998
	A15	5,811,451		Minoia, et al.	09-22-1998
	A16	5,866,164		Kuczynski, et al.	02-02-1999
	A17	5,958,452		Oshlack, et al.	09-28-1999
	A18	5,972,954	·	Foss, et al.	10-26-1999
	A19	6,096,756		Crain, et al.	08-01-2000
	A20	6,194,382	B1	Crain, et al.	02-27-2001
	A21	6,261,599	B1	Oshlack, et al.	07-17-2001
	A22	6,274,591	B1	Foss, et al.	08-14-2001
	A23	6,395,705	B2	Crain, et al.	05-28-2002
	A24	6,419,959	B1	Walter, et al.	07-16-2002
	A25	6,451,806	B2	Farrar	09-17-2002
	A26	6,559,158	B1	Foss, et al.	05-06-2003
1/	A27	6,608,075	B1	Foss, et al.	08-19-2003
	A28	RE36,547		Crain, et al.	02-01-2000
MG	A29	2002/0188005	Al	Farrar, et al.	12-12-2002

FOREIGN PATENT DOCUMENTS

Examiner's	Cite	Foreign Patent Document		ment	Name of Patentee or Applicant of Cited	Publication of Translation	Translation
Initials	No.	Office/ Country	Number	Kind Code	Document (not necessary)	Cited Document MM-DD-YYYY	(Y/N)
MG	B1	AU	610,561		Shelley	08-17-1988	
MG	B2_	CA	1,315,689		The University of Chicago	04-06-1993	
MG	В3	EP	0278821	A1	Shelly (Abstract)	08-17-1988	

FORM PTO	0-1449/A and B (M	lodifie	d)	APPLICATION NO.:	10/821,813	ATTY. DOCKET NO.: P0453.70112US01
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STATEMENT BY APPLICANT			LICANT	APPLICANT:	Boyd et al.	
				GROUP ART UNIT:	Not Vet Assigned	EXAMINER: Not Yet Assigned
Sheet	2	of	6		110t Tet 71331g.10d	EAST AVAILABLE TO THE TEST BOOK TO THE T

MG	B4	EP	0352361	Al	The Rockefeller University	01-31-1990	
1	B5	EP	278,821	Al	Marc Yves Shelly (Derwent Abstract)	08-17-1988	
	B6	EP	306,575	B1	The Univ. of Chicago	03-15-1989	
	B7	EP	352,361	Al	The Rockefeller University	01-31-1990	
	B8	EP	760,661	Bl	Minoia, et al.	12-30-1998	
	B9	JР	2,625,457	B2	Goldberg (Derwent Abstract)	07-02-1997	
	B10	NZ	222,911		The Univ. of Chicago	12-14-1987	
1	B11	wo	83/03197	A1	The Rockefeller University	09-29-1983	
	B12	wo	88/05297	A1	Shelly	07-28-1988	
·	B13	wo	95/31985	A2	Minoia, et al.	11-30-1995	
	B14	wo	97/33566		Alza Corp.	09-18-1997	
	B15	wo	98/25613		Klinge Pharma GmbH	06-18-1998	Yes
	B16	wo	01/13909	A2	Critical Care Pharm.	03-01-2001	
	B17	wo	01/37785	A2	Adolor Corp.	05-31-2001	
	B18	wo	01/41705	A2	Adolor Corp.	06-14-2001	
	B19	wo	01/42207	A2	Adolor Corp.	06-14-2001	
V	B20	wo	01/85257	A2	Pain Therapeutics, Inc	11-15-2001	
MG	B21	wo	02/060870	A2	Adolor Corp.	08-08-2002	

OTHER ART — NON PATENT LITERATURE DOCUMENTS

Examiner's	Cite	Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item	Translati	ion
Initials	No	(book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s), publisher, city and/or country where published.	(Y/N))
140		AKINBAMI et al., Effect of a peripheral and a central acting opioid antagonist on the testicular response to		
MG	C1	stress in rats. Neuroendocrinology. 1994 Apr;59(4):343-8.		
ı		AMIN et al., Efficacy of methylnaltrexone versus naloxone for reversal of morphine-induced depression of		
	C2	hypoxic ventilatory response. Anesth Analg. 1994 Apr;78(4):701-5.		
		AMIR, Naloxone improves, and morphine exacerbates, experimental shock induced by release of endogenous		
	C3	histamine by compound 48/80. Brain Res. 1984 Apr 9;297(1):187-90.		
	C4	AMIR et al., Endorphins in endotoxin-induced hyperglycemia in mice. Arch Toxicol Suppl. 1983;6:261-5.		
		ARGENTIERI et al., Interaction of the opiate antagonist, naltrexone methyl bromide, with the acetylcholine		
	C5	receptor system of the motor end-plate. Brain Res. 1983 Oct 31;277(2):377-9.		_
<u> </u>		BARATTI et al., Brain opioid peptides may participate in the reversal of pentylenetetrazol-induced amnesia.		
	C6	Methods Find Exp Clin Pharmacol. 1990 Sep;12(7):451-6.		
		BEDINGFIELD et al., Methylnaltrexone attenuates taste aversion conditioned by low-dose ethanol. Alcohol.		
	C7	1998 Jan;15(1):51-4.		
		BIANCHETTI et al., Quaternary derivatives of narcotic antagonists: stereochemical requirements at the chiral		
	C8	nitrogen for in vitro and in vivo activity. Life Sci. 1983;33 Suppl 1:415-8.	 	_
		BIANCHI et al., Quaternary narcotic antagonists' relative ability to prevent antinociception and gastrointestinal		
]		transit inhibition in morphine-treated rats as an index of peripheral selectivity. Life Sci. 1982 May		
	C9	31;30(22):1875-83.		_
	040	BICKEL, Stimulation of colonic motility in dogs and rats by an enkephalin analogue pentapeptide. Life Sci.	1 1	
	C10	1983;33 Suppl 1:469-72.	 	_
		BLANK et al., Central, stereoselective receptors mediate the acute effects of opiate antagonists on luteinizing		
	C11	hormone secretion. Life Sci. 1986 Oct 27;39(17):1493-99.		_
W	040	BRIX-CHRISTENSEN et al., Endogenous morphine is produced in response to cardiopulmonary bypass in		
	C12	neonatal pigs. Acta Anaesthesiol Scand. 2000 Nov;44(10):1204-8.	 -	
MG		BROWN et al., Opiate antagonists: central sites of action in suppressing water intake of the rat. Brain Res. 1981		
	C13	Sep 28;221(2):432-6.		_

FORM PTC)-1449/A and B (M	Iodifie	d)	APPLICATION NO.:	10/821,813	ATTY. DOCKET NO.: P0453.70112US01
	RMATION I			FILING DATE:	April 8, 2004	CONFIRMATION NO.: Not Yet Assigned
STAT	EMENT BY	APP	LICANT	APPLICANT:	Boyd et al.	
				GROUP ART UNIT:	Not Yet Assigned	EXAMINER: Not Yet Assigned
Sheet.	3	of	6		, , , , , , , , , , , , , , , , , , ,	

MG	C14	BROWN et al., Reversal of morphine-induced catalepsy in the rat by narcotic antagonists and their quaternary derivatives. Neuropharmacology. 1983 Mar;22(3):317-21.	
	C15	BROWN et al., The use of quaternary narcotic antagonists in opiate research. Neuropharmacology. 1985	
	1015	Mar;24(3):181-91. Review. CALCAGNETTI et al., Quaternary naltrexone reveals the central mediation of conditional opioid analgesia.	
	C16	Pharmacol Biochem Behav. 1987 Jul;27(3):529-31.	
		CHANG et al., An antiabsorptive basis for precipitated withdrawal diarrhea in morphine-dependent rats. J	
	C17	Pharmacol Exp Ther. 1984 Feb;228(2):364-9.	
		CULPEPPER-MORGAN et al., Treatment of opioid-induced constipation with oral naloxone: a pilot study. Clin	ľ
	C18	Pharmacol Ther. 1992 Jul;52(1):90-5 (ABSTRACT ONLY).	
ĺ	040	EISENBERG, Effects of naltrexone on plasma corticosterone in opiate-naive rats: a central action. Life Sci.	
	C19	1984 Mar 19;34(12):1185-91. FERNANDEZ-TOME et al., Interaction between opioid agonists or naloxone and 5-HTP on feeding behavior in	
•	C20	food-deprived rats. Pharmacol Biochem Behav. 1988 Feb;29(2):387-92.	
	<u> </u>	FOSS, A review of the potential role of methylnaltrexone in opioid bowel dysfunction. Am J Surg. 2001	
	C21	Nov;182(5A Suppl):19S-26S. Review.	
	1021	FOSS et al., 1995 Annual scientific meeting of the American Society of Anesthesiologists. Atlanta, Georgia,	
1.	.C22	October 21-25, 1995. Abstracts. Anesthesiology. 1995 Sep;83(3A Suppl):A361.	
_	1.022	FOSS et al., Prevention of apomorphine- or cisplatin-induced emesis in the dog by a combination of	
- 1	C23	methylnaltrexone and morphine. Cancer Chemother Pharmacol. 1998;42(4):287-91.	
_	1	FOSS et al., Safety and tolerance of methylnaltrexone in healthy humans: a randomized, placebo-controlled,	
	C24	intravenous, ascending-dose, pharmacokinetic study. J Clin Pharmacol. 1997 Jan;37(1):25-30.	
		FOSS et al., Dose-related antagonism of the emetic effect of morphine by methylnaltrexone in dogs. J Clin	
1	C25	Pharmacol. 1993 Aug;33(8):747-51.	
		FOSS et al., Effects of methylnaltrexone on morphine-induced cough suppression in guinea pigs. Life Sci.	1
	C26	1996;59(15):PL235-8.	
		FOSS et al., Methylnaltrexone reduces morphine-induced postoperative emesis by 30%. Anesth Analg.	
	C27	1994;78:S119.	
	000	FRANCE et al., Comparison of naltrexone and quaternary naltrexone after systemic and intracerebroventricular	İ
	C28	administration in pigeons. Neuropharmacology. 1987 Jun;26(6):541-8. FRANCE et al., Intracerebroventricular drug administration in pigeons. Pharmacol Biochem Behav. 1985	
	C29		
	029	Nov;23(5):731-6. FRIEDMAN et al., Opioid antagonists in the treatment of opioid-induced constipation and pruritus. Ann	
	C30	Pharmacother. 2001 Jan;35(1):85-91. Review.	
	1030	GMEREK et al., Independent central and peripheral mediation of morphine-induced inhibition of	
	C31	gastrointestinal transit in rats. J Pharmacol Exp Ther. 1986 Jan;236(1):8-13.	
	1001	HEIN et al., Pharmacological analysis of the discriminative stimulus characteristics of ethylketazocine in the	
	C32	rhesus monkey. J Pharmacol Exp Ther. 1981 Jul;218(1):7-15.	
	C33	HOWD et al., Naloxone and intestinal motility. Experientia. 1978 Oct 15;34(10):1310-1.	
-	+	JALOWIEC et al., Suppression of juvenile social behavior requires antagonism of central opioid systems.	
	C34	Pharmacol Biochem Behav. 1989 Jul;33(3):697-700.	
		JANKOVIC et al., Quaternary naltrexone: its immunomodulatory activity and interaction with brain delta and	
	C35	kappa opioid receptors. Immunopharmacology. 1994 Sep-Oct;28(2):105-12.	
		KAUFMAN et al., Role of opiate receptors in the regulation of colonic transit. Gastroenterology. 1988	
	C36	Jun;94(6):1351-6.	
		KIM et al., Assay for methylnaltrexone in rat brain regions and serum by high-performance liquid	
—	C37	chromatography with coulometric electrochemical detection. Chromatographia. 1989 Oct;28(7-8):359-63.	
	000	KINSMAN et al., Effect of naloxone on feedback regulation of small bowel transit by fat. Gastroenterology.	
	C38	1984 Aug;87(2):335-7.	
	Can	KOBLISH et al., Behavioral profile of ADL 8-2698, a novel GI-restricted μ opioid receptor antagonist. Society]
+	C39	for Neuroscience Abstracts. 2001;27(2):2407. KOBYLECKI et al., N-Methylnalorphine: definition of N-allyl conformation for antagonism at the opiate	
¥	C40	receptor. J Med Chem. 1982 Nov;25(11):1278-80.	
MG	C41	KOCZKA, et al., Acta Chimica Academica Scien. Hung. (1967) 51(4), 393-02	

FORM PTO	D-1449/A and B (M	Iodifie	d)	APPLICATION NO.:	10/821,813	ATTY. DOCKET NO.: P0453.70112US01
	RMATION I			FILING DATE:	April 8, 2004	CONFIRMATION NO.: Not Yet Assigned
STATEMENT BY APPLICANT			APPLICANT:	Boyd et al.		
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Sheet	4	of	6	GROOF ART ONT.	Not Tet Assigned	EARWINGE. Not be Assigned

MG	C42	KOOB et al., Effects of opiate antagonists and their quaternary derivatives on heroin self-administration in the rat. J Pharmacol Exp Ther. 1984 May;229(2):481-6.		
ı	C43	KOTAKE et al., Variations in demethylation of N-methylnaltrexone in mice, rats, dogs, and humans.		_
		Xenobiotica. 1989 Nov;19(11):1247-54. KROMER et al., Endogenous opioids, the enteric nervous system and gut motility. Dig Dis. 1990;8(6):361-73.		
	C44	Review. KROMER et al., The current status of opioid research on gastrointestinal motility. Life Sci. 1989;44(9):579-89.		
	C45	Review.		
_	C46	LEANDER, A kappa opioid effect: increased urination in the rat. J Pharmacol Exp Ther. 1983 Jan;224(1):89-94.		_
	C47	LITTLE, et al., Society for Neuroscience Abstracts, 27 (2); 2001, p. 2407		_
	C48	LIVINGSTON et al., Postoperative ileus. Dig Dis Sci. 1990 Jan;35(1):121-32. Review.		_
	C49	LYDON et al., ESA Free Paper Prize Competition. Eur J Anaesthesiol. 2001 Apr;18 Suppl 21:92.		_
	C50	LYSLE et al., Modulation of immune status by a conditioned aversive stimulus: evidence for the involvement of endogenous opioids. Brain Behav Immun. 1992 Jun;6(2):179-88.		
	C51	MAGNAN et al., The binding spectrum of narcotic analgesic drugs with different agonist and antagonist properties. Naunyn Schmiedebergs Arch Pharmacol. 1982 Jun;319(3):197-205.		_
	C52	MANARA, et al., Adv. Endog. Exog. Opioids, Poroc. Int. Narc. Res. Conf., 12th (1981), 402-4		-
_	C53	MANARA et al., The central and peripheral influences of opioids on gastrointestinal propulsion. Annu Rev Pharmacol Toxicol. 1985;25:249-73. Review.		-
		MICKLEY et al., Quaternary naltrexone reverses morphine-induced behaviors. Physiol Behav. 1985		_
	C54	Aug;35(2):249-53. MISRA et al., Intravenous kinetics and metabolism of [15,16-3H]naltrexonium methiodide in the rat. J Pharm		_
	C55	Pharmacol. 1987 Mar;39(3):225-7.		
		MOERMAN et al., Evaluation of methylnaltrexone for the reduction of postoperative vomiting and nausea		
	C56	incidences. Acta Anaesthesiol Belg. 1995;46(3-4):127-32.		
	C57	MOSS, et al., N. Engl. J. Med., (2002) 346 (6), 455	\rightarrow	_
	050	MUCHA, Is the motivational effect of opiate withdrawal reflected by common somatic indices of precipitated	- 1	
	C58	withdrawal? A place conditioning study in the rat. Brain Res. 1987 Aug 25;418(2):214-20.		_
	C59	MUCHA, Taste aversion involving central opioid antagonism is potentiated in morphine-dependent rats. Life Sci. 1989;45(8):671-8.		
	C60	MURPHY et al., Anesthesiology, Sept. (1999), 91 (3A) p. A349 (Abstract)		_
	+	MURPHY et al., Pharmacokinetic profile of epidurally administered methylnaltrexone, a novel peripheral opioid		_
	C61	antagonist in a rabbit model. Br J Anaesth. 2001 Jan;86(1):120-2.		
		MURPHY et al., American Society of Anesthesiologists 1999 annual meeting. Dallas, Texas, USA. October 9-		_
	C62	13, 1999. Abstracts. Anesthesiology. 1999 Sep;91(3A Suppl):A349.		
	C63	MURPHY et al., Opioid-induced delay in gastric emptying: a peripheral mechanism in humans. Anesthesiology. 1997 Oct;87(4):765-70.		
	C64	MURPHY et al., Opioid antagonist modulation of ischaemia-induced ventricular arrhythmias: a peripheral mechanism. J Cardiovasc Pharmacol. 1999 Jan;33(1):122-5.		
	C65	NARANJO et al., Evidence for a central but not adrenal, opioid mediation in hypertension induced by brief isolation in the rat. Life Sci. 1986 May 26;38(21):1923-30.		
	C66	NELSON, Dissertation Abstracts International, (62/03-B), p. 1635 (Abstract)		_
	C67	ODIO et al., Central but not peripheral opiate receptor blockade prolonged pituitary-adrenal responses to stress. Pharmacol Biochem Behav. 1990 Apr;35(4):963-9.		_
		OSINSKI et al., Determination of methylnaltrexone in clinical samples by solid-phase extraction and high-		
	C68	performance liquid chromatography for a pharmacokinetics study. J Chromatogr B Analyt Technol Biomed Life Sci. 2002 Nov 25;780(2):251-9.		
		PAPPAGALLO, Incidence, prevalence, and management of opioid bowel dysfunction. Am J Surg. 2001		
	C69	Nov;182(5A Suppl):11S-18S. Review.		_
	C70	POLAK et al., Enkephalin-like immunoreactivity in the human gastrointestinal tract. Lancet. 1977 May 7;1(8019):972-4.		
V	C71	POWELL et al., Paradoxical effects of the opioid antagonist naltrexone on morphine analgesia, tolerance, and reward in rats. J Pharmacol Exp Ther. 2002 Feb;300(2):588-96.		
MG	C72	QUOCK, et al, J. Bioelectr. (1986), 5(1), 35-46		-

FORM PTO-1449/A and B (Modified)				APPLICATION NO.:	10/821,813	ATTY. DOCKET NO.: P0453.70112US01
	RMATION D	_		FILING DATE:	April 8, 2004	CONFIRMATION NO.: Not Yet Assigned
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Sheet	5	of	6	GROOT FART OWN:	Tiot Tet Tissigned	Die Leiter 100 100 100 100 100 100 100 100 100 10

MG	C73	QUOCK et al., Narcotic antagonist-induced hypotension in the spontaneously hypertensive rat. Life Sci. 1985 Sep 2:37(9):819-26.	
	C74	QUOCK et al., Narcotic antagonist potentiation of apomorphine drug effect: a stereospecific, centrally mediated drug action. Prog Neuropsychopharmacol Biol Psychiatry. 1985;9(3):239-43.	
	0/4	RAMABADRAN, Effects of N-methylnaloxone and N-methylnaltrexone on nociception and precipitated	
1	C75	abstinence in mice. Life Sci. 1982 Sep 20-27;31(12-13):1253-6.	
	10,0	RIVIÈRE et al., Fedotozine reverses ileus induced by surgery or peritonitis: action at peripheral kappa-opioid	
	C76	receptors. Gastroenterology. 1993 Mar;104(3):724-31.	- 1
	C77	ROBINSON et al., Oral naloxone in opioid-associated constipation. Lancet. 1991 Aug 31;338(8766):581-2.	
	-	ROGER et al., Colonic motor responses in the pony: relevance of colonic stimulation by opiate antagonists. Am	
	C78	J Vet Res. 1985 Jan;46(1):31-5.	
		RUSSELL et al., Antagonism of gut, but not central effects of morphine with quaternary narcotic antagonists.	.
<u> </u>	C79	Eur J Pharmacol. 1982 Mar 12;78(3):255-61.	
1	000	SCHAEFER et al., Effects of opioid antagonists and their quaternary derivatives on locomotor activity and fixed	İ
	C80	ratio responding for brain self-stimulation in rats. Pharmacol Biochem Behav. 1985 Nov;23(5):797-802.	
	C81	SCHANG et al., Beneficial effects of naloxone in a patient with intestinal pseudoobstruction. Am J Gastroenterol. 1985 Jun;80(6):407-11.	
	1001	SCHANG et al., How does morphine work on colonic motility? An electromyographic study in the human left	
	C82	and sigmoid colon. Life Sci. 1986 Feb 24;38(8):671-6.	
	+	SCHILLER et al., Studies of the mechanism of the antidiarrheal effect of codeine. J Clin Invest. 1982	
	C83	Nov;70(5):999-1008.	
	C84	SCHMIDHAMMER, et al., Helv. Chim. Acta (1994), Vol. 77, No. 6, p. 1585-9	
	C85	SCHMIDHAMMER, et al., Helv. Chim. Acta. (1993) No. 1, p. 476-80	
	C86	SCHOLZ, 2000, 63 (6) p. 103	
		SCHREIER et al., Central regulation of intestinal function: morphine withdrawal diarrhea. Proc West Pharmacol	
	C87	Soc. 1982;25:151-4.	
		SOLVASON et al., Naltrexone blocks the expression of the conditioned elevation of natural killer cell activity in	
	C88	BALB/c mice. Brain Behav Immun. 1989 Sep;3(3):247-62.	
	C89	SWAN, et al., AIDS Research, NIDA Notes, (1995), 10(3), 1-6	
	C90	SYKES, Oral naloxone in opioid-associated constipation. Lancet. 1991 Jun 15;337(8755):1475.	
	C01	TAGUCHI et al., Selective postoperative inhibition of gastrointestinal opioid receptors. N Engl J Med. 2001 Sep	
	C91	27;345(13):935-40. THOMPSON et al., Opioid stimulation in the ventral tegmental area facilitates the onset of maternal behavior in	
	C92	rats. Brain Res. 1996 Dec 16;743(1-2):184-201.	
_	1002	UKAl et al., Suppression of deprivation-induced water intake in the rat by opioid antagonists: central sites of	
	C93	action, Psychopharmacology (Berl), 1987;91(3):279-84.	
		VALENTINO et al., Quaternary naltrexone: evidence for the central mediation of discriminative stimulus effects	
	C94	of narcotic agonists and antagonists. J Pharmacol Exp Ther. 1981 Jun;217(3):652-9.	
	00-	VALENTINO et al., Receptor binding, antagonist, and withdrawal precipitating properties of opiate antagonists.	
	C95	Life Sci. 1983 Jun 20;32(25):2887-96.	
	C96	WALKER, et al., Psychopharmacology (1991), 104(2), p. 164-6	
	C97	WARREN et al., Effects of quaternary naltrexone and chlordiazepoxide in squirrel monkeys with enhanced sensitivity to the behavioral effects of naltrexone. J Pharmacol Exp Ther. 1985 Nov;235(2):412-7.	
	C98	WILLETTE, et al., Res. Commun. Subst. Abuse (1983), 4(4), 325-37	
		YUAN et al., Drug Dev. Res. (2000) 50(2), 133-141	
	C99	YUAN et al., Gastric effects of methylnaltrexone on mu, kappa, and delta opioid agonists induced brainstem	
1	C100	unitary responses. Neuropharmacology. 1999 Mar;38(3):425-32.	
	C101	YUAN et al., Anesthesiology, Sept. (1995), 83 (3A), p A358 (Abstract)	
	C102	YUAN et al., Anesthesiology, Sept. (1995), 83 (3A), p A360 (Abstract)	+
+	C102	YUAN et al., Anesthesiology, Sept. (1999), 91 (3A) p. A973 (Abstract)	-+
\	0103	YUAN et al., Alesthesiology, Sept. (1999), 91 (3A) p. A973 (Adstract) YUAN et al., Effects of enteric-coated methylnaltrexone in preventing opioid-induced delay in oral-cecal transit	
V	C104	time. Clin Pharmacol Ther. 2000 Apr;67(4):398-404.	
	+	YUAN et al., The safety and efficacy of oral methylnaltrexone in preventing morphine-induced delay in oral-	
MG	C105	cecal transit time. Clin Pharmacol Ther. 1997 Apr,61(4):467-75.	- 1

FORM PTO-1449/A and B (Modified)	APPLICATION NO.:	10/821,813	ATTY. DOCKET NO.: P0453.70112US01
INFORMATION DISCLOSURE	FILING DATE:	April 8, 2004	CONFIRMATION NO.: Not Yet Assigned
STATEMENT BY APPLICANT .	APPLICANT:	Boyd et al.	
	GROUP ART UNIT:	Not Yet Assigned	EXAMINER: Not Yet Assigned
Sheet 6 of 6			

N	1G C106	YUAN et al., Methylnaltrexone prevents morphine-induced delay in oral-cecal transit time without affecting analgesia: a double-blind randomized placebo-controlled trial. Clin Pharmacol Ther. 1996 Apr;59(4):469-75.	
	C107	YUAN, et al., Clinical Pharmacology & Therapeutics (1995) 57(2), p. 138	
	C108	YUAN et al., Efficacy of orally administered methylnaltrexone in decreasing subjective effects after intravenous morphine. Drug Alcohol Depend. 1998 Oct 1;52(2):161-5.	
	C109	YUAN et al., Effects of methylnaltrexone on morphine-induced inhibition of contraction in isolated guinea-pig ileum and human intestine. Eur J Pharmacol. 1995 Mar 24;276(1-2):107-11.	
	C110	YUAN et al., Effects of subcutaneous methylnaltrexone on morphine-induced peripherally mediated side effects: a double-blind randomized placebo-controlled trial. J Pharmacol Exp Ther. 2002 Jan;300(1):118-23.	
•	C111	YUAN et al., Oral methylnaltrexone for opioid-induced constipation. JAMA. 2000 Sep 20;284(11):1383-4.	
	C112	YUAN et al., Methylnaltrexone for reversal of constipation due to chronic methadone use: a randomized controlled trial. JAMA. 2000 Jan 19;283(3):367-72.	
•	C113	YUAN et al., Effects of intravenous methylnaltrexone on opioid-induced gut motility and transit time changes in subjects receiving chronic methadone therapy: a pilot study. Pain. 1999 Dec;83(3):631-5.	
	C114	YUAN et al., Effects of methylnaltrexone on chronic opioid induced gut motility and transit time changes. Br J Anaesth. 1998;81(1):94.	
V	C115	YUAN et al., Effects of methylnaltrexone on chronic opioid-induced gut motility and transit time changes. University of Leicester – Abstracts from the Eighth International Symposium on Pain, Anaesthesia and Endocrinology. 1997 September 18-19th.	
MC	G C116	[No Author Listed] Oncology. 1996;10(12):1880.	

EXAMINER /Michel Graffeo/	DATE CONSIDERED	12/06/2006
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#EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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